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ORIGINAL ARTICLE

ULTRASONOGRAPHIC OPTIC NERVE SHEATH DIAMETER MEASUREMENT FOR RAISED INTRACRANIAL PRESSURE IN A TERTIARY CARE CENTRE OF A DEVELOPING COUNTRY

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Background: Intracranial hypertension is not an uncommon life-threatening syndrome, caused by a variety of non-neurological and neurological illnesses, and quick diagnosis, timely treatment of Raised Intracranial Pressure (ICP) is associated with improved outcome. Our aim of study was to determine ultrasonographic measurement of Optic nerve sheath diameter (ONSD) for raised ICP. **Methods**: Prospective case series done in Emergency and Paediatric critical care unit of Aga Khan University Hospital. ONSD measurement in millimetres was done by placing linear probe of ultrasound on eye ball. **Results**: Forty-eight patients were included in study with mean age of 7.5±5.0 years with 21/48 (43.8%) between 1–8 years and 19/48 (39.6%) >8 years with 32/48 (66.7%) were male. Non-traumatic coma was most common diagnosis 41/48 (85.4%) with infectious cause being most common while Traumatic brain injury constitutes 7/48 (14.6%). Ct scan brain was done in 39/48 (81.3%) while MRI brain in rest of patients. Raised ICP was found in 83.33% (40/48) patients with Ultrasonographic ONSD measurement as compared to CT scan/MRI 14/48 (29.2%). 85% of patients, showed ultrasonographic ONSD measurement suggestive of Raised ICP with GCS ≤12. Mean ONSD with signs of raised ICP in infants 4.64 (±0.48), in 1–10 years 6.44 (±0.65), and in adolescent >10 years 6.28 (±0.62) ONSD respectively with ROC Curve showing Area Under Curve (AUC) 0.814 (95% CI, 0.692-0.936). **Conclusion**: We identified threshold of Ultrasonographic ONSD measurement in infants >4.0 mm, in children 1–10 yrs >4.71 mm, in adolescent >10 yrs >5.43 mm for raised ICP with sensitivity and specificity of 100% and 60–66.7% respectively. 85% of patients showed raised ICP with Ultrasonographic ONSD measurement with GCS ≤12.

Keywords: Ultrasonography, Optic nerve sheath diameter, Raised Intracranial Pressure, Paediatric intensive care unit

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INTRODUCTION

Intracranial hypertension is not an uncommon life threatening syndrome, which is caused by a variety of non-neurological and neurological illnesses, and quick diagnosis and timely treatment of Raised Intracranial Pressure (ICP) is associated with improved outcome.[1] Although the invasive devices (Intraparenchymal, Intraventricular, subdural, epidural) for raised ICP monitoring remain the gold standard,[2,3] but it is invasive and not always possible due to lack of availability of neurosurgeon in all hospital settings or contraindications such as thrombocytopenia or coagulopathy,[4] and also it is responsible for multiple complications such as intracranial haemorrhages[5] in 1.1–5.8% of cases,[4] mal functioning[5] in 6.3–40% of cases,[4] or various infections[6] in 0–15% of cases[4]. However, Magnetic Resonance Imaging (MRI) and Computed tomography (CT) scan brain may be used to assess the increased ICP but they are costly, needs lengthy time to be done, have restricted availability, and more over necessitate dangerous patient transport in scenarios when patient is critically ill to be transported, also poor performance had been reported for CT scan brain for the identification of increased ICP.[7,8] Even with normal CT scan the diagnosis of raised ICP ranges from 0–88%.[9] Ultrasonographic Optic Nerve Sheath Diameter (ONSD) measurement is now becoming a simple bedside tool broadly used because of its low cost, and readily availability.[10] In the critical care environment, ultrasonographic optic nerve sheath diameter measurement has ignited significant recent interest, due to its non-invasiveness, repeatable and quickly performed at bed side which makes it a valuable bedside diagnostic tool. Therefore, we aim to determine if ultrasonographic optic nerve sheath diameter measurement accurately predict raised ICP. The objective of this study was to determine whether the ultrasonographic Optic Nerve Sheath Diameter measurement can predict the raised ICP.

MATERIAL AND METHODS

This case series was completed over six-month period from 1st September 2014 to 28 February 2015 after the approval from Ethical review committee of Aga Khan University Hospital. Setting included Emergency room (ER) and paediatric intensive care unit (PICU) of Aga Khan University Hospital, Karachi. Ethical review committee of Aga Khan University Hospital approved the study (2747-Ped-ERC-13). All data was recorded on password protection and confidentiality was maintained by using Code Numbers.

Inclusion Criteria:

All children from age 1 month -16 years with the following inclusion criteria[10] was included in the study

- Traumatic brain injury defined as a moderate with GCS 9-13
- Traumatic brain Injury defined as a sever with GCS <9
- Active malignancy history with new onset neurological symptoms.
- Raised ICP clinical signs e.g. Anisocoric pupils, motor posturing, Cushing triad.
- From ER to admission with Progressive neurological deterioration

Exclusion Criteria:

Patients with orbital trauma with orbital fractures, orbital tumor, and intraocular space occupying lesions were excluded from the study.

The method for measurement of ultrasonographic ONSD was described in literature.[1,11] We used a probe of 7.5 MHz linear array of ultrasound machine of Mindray. The depth was set to 5–6 cm. The probe was covered with gloves easily available with gel placed in it to prevent gel contact with the eyes which in turn prevent any reaction or possibility of infection with in the eye. The probe was then positioned over the closed eye, over the upper eyelid of the supine patient with head end elevated at 30 degrees in axial plane as shown in figure-1.[12]

Two hyperechoec lines behind the globe was identified as optic nerve sheath. Almost, 3 mm behind the papilla, which suggested the best dispensability, maximum U/S contrast and high reproducibility was the point of measurement of outer limit of hyperechoec line using electronic callipers as shown in figure-2.[12,13] We considered the upper limit for ONSD of 4 mm in age <1 yrs, 4.5 mm between 1–10 years and >5 mm in age >10 years and were considered as a sign of raised ICP as consistent with recent literature.[14–18] Measurements was taken in both eyes in the Emergency Room (ER) or Paediatric Intensive Care Unit(PICU) by an experienced trained physician or Intensive care fellow having experience of measurement of ONSD previously. Our Hospital ER and PICU have its own U/S machine available. Basic demographic data including age gender and weight with primary and associated diagnosis was collected after taking informed consent. Clinical indication for ONSD and CT scan findings were also collected as in proforma for patients in ER or PICU who met the inclusion criteria. The ultrasonographic optic nerve sheath diameter measurement was documented on structured proforma, and operator took 3 readings on each side and the sum will be calculated to get the mean and transferred to SPSS 20 for the analysis.

It includes measurement of mean ± standard deviation for continuous variables and frequencies of all categorical variables. ONSD of 4 mm in age <1year, 4.5 mm between 1–10 yrs and >5 mm in age >10 years was considered as a sign of raised ICP as in previous studies.[14–18] Sensitivity, specificity, Positive predicted Value, and Negative predicted vale was calculated accordingly.[19] ROC curve was made for ultrasonographic ONSD measurements in patients with clinical signs of raised ICP, in all age groups.

RESULTS

Over all, in the study, 48 patients were included, with mean age 7.5 years (±5) with 32 (66.7%) were male. Among these patients, 21 (43.8%) were between 1–10 years and 19 (39.6%) were >10 years of age. Most of the patients presented with non-traumatic coma with primary neurological disorder mainly meningeoencephalitis 27 (56.25%) followed by stroke 7 (14.5%) as shown in table-1. Patients with GCS ≤12 constituted 87.5% (40/48), 85% of them showed ONSD measurement suggestive of Raised ICP. In majority of patients CT Scan brain 39 (81.2%) was done, and MRI brain in 9 (18.8%). The most common indication for imaging among these patients includes Clinical signs of raised ICP with progressive neurological deterioration 26 (54.2%) followed by progressive neurological deterioration alone as shown in table-1.

CT scans Brain/ MRI Brain of 14 (29.2%) patients were suggestive of raised ICP as compared to ultrasonographic ONSD measurement 40 (83.33%). Also 85% of patients with GCS ≤12 showed ultrasonographic ONSD measurement suggestive of Raised ICP. The CT scan brain and MRI brain findings suggestive of raised ICP were shown in figure-3. The mean values of ultrasound guided ONSD measurement for 3 age groups were shown in table-2.

We identified threshold of Ultrasonographic ONSD measurement in infants >4.0 mm, in children

1–10 yrs >4.71 mm, in adolescent >10 yrs >5.43 mm for raised ICP with sensitivity and specificity of 100% and 60–66.7% respectively, with positive predictive value of 100% and negative predictive value 35%. The ROC curve at various threshold of ultrasonographic ONSD measurement for clinical signs of raised ICP with Area under Curve (AUC) 0.814 (95% CI, 0.692–0.936) is shown in figure-4.

Figure-5.1, 5.2, and 5.3 showed the ROC curves at various age groups. The thresholds of Ultrasonographic ONSD measurement for the identification of raised ICP with respect to various age groups are shown in table-3.

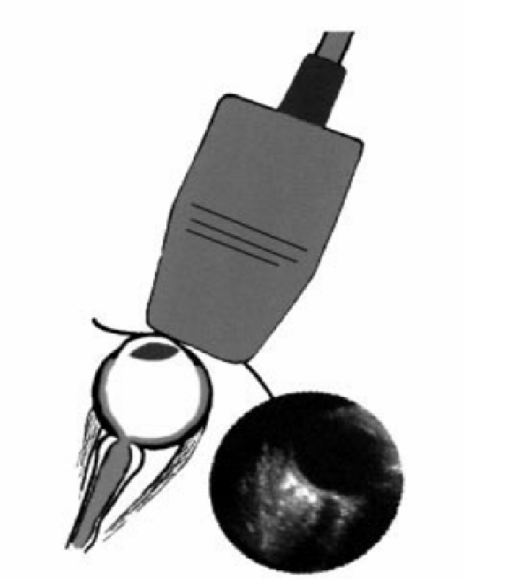

Figure-1: The probe was then positioned over the closed eye, over the upper eyelid of the supine patient[12]

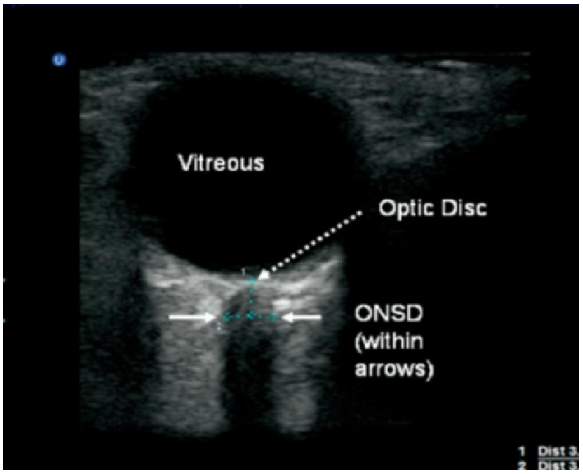

Figure-2: The technique of ocular ultrasound and the image with the cursors set at 3 mm behind the globe to measure the optic nerve sheath diameter[12]

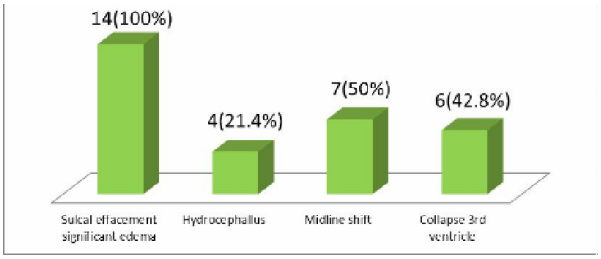

Figure-3: CT Scan/MRI brain finding suggestive of raised intracranial pressure.

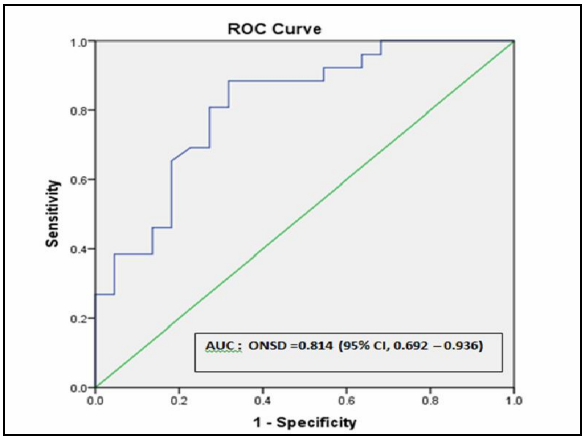

Figure-4: ROC curve at various thresholds ONSD measurement at all ages

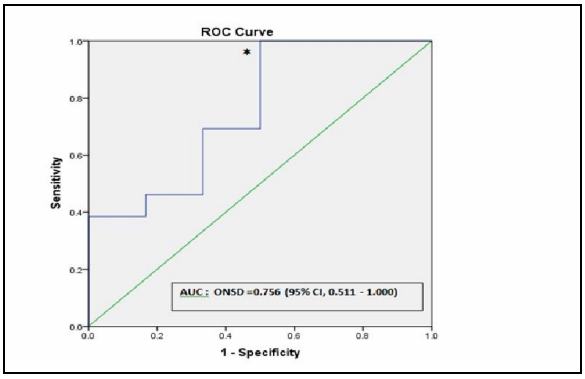

Figure-5.1: ROC curve at various thresholds ONSD measurement for patients >10 years of age

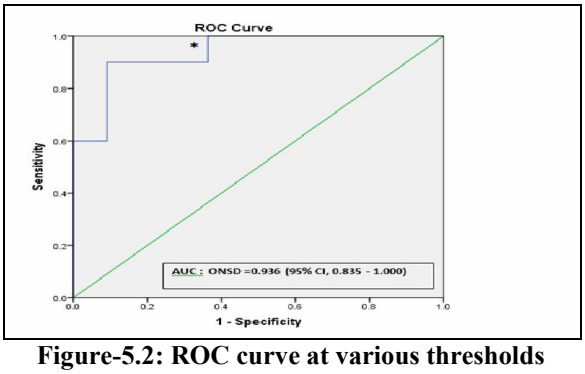

Figure-5.2: ROC curve at various thresholds ONSD measurement for patient 1–10 years of age

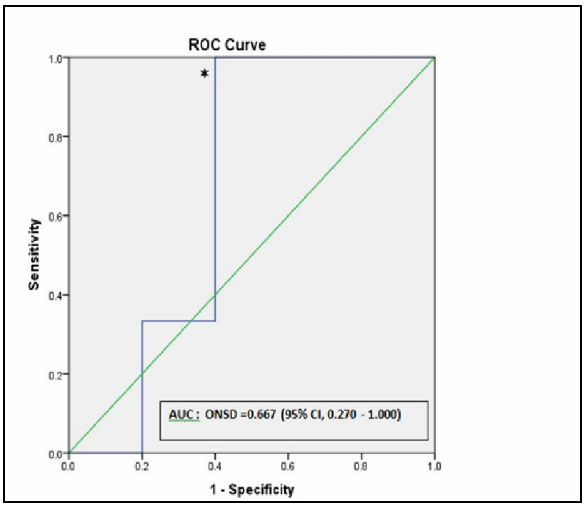

Figure-5.3: ROC curve at various thresholds ONSD measurement for patients <1 year of age

Table-1: Characteristics of patients

Characteristics	n=48(%)
Age (yrs) mean +/-SD	7.5 (±5)
< 1 yrs	8 (16.7)
1-10 yrs	21 (43.8)
>10 yrs	19 (39.6)
Gender	
Male	32 (66.7)
Female	16 (33.3)
Categories	
Traumatic brain injury	7 (14.6)
Road traffic accidents	6 (12.5)
Blast injury	1 (2.08)
Non-Traumatic Coma	41 (85.4)
Primary Neurological injury	37 (75.5)
Meningeoencephalitis	27 (56.25)
Stroke	7 (14.5)
Status Epilepticus	2 (1.16)
Space occupying lesion	1 (2.08)
Secondary neurological injury	4 (8.33)
Diabetic Ketoacidosis	2 (4.16)
Wilson Disease	1 (2.08)
Hemolytic uremic syndrome	1 (2.08)
GCS	
≤12	42 (87.5)
>12	6 (12.5)
Clinical Indication for imaging	
Moderate TBI	4 (8.33)
Sever TBI	4 (8.33)
Clinical Signs of Raised ICP	2 (4.16)
Clinical Signs + progressive neurological deterioration	24 (50)
Progressive neurological deterioration	14 (29.1)
Imaging	
CT Scan brain	39 (81.2)
MRI brain	9 (18.8)
Clinical signs suggestive of raised ICP	26 (54.2)
CT Scan/MRI brain suggestive of raised ICP	14 (29.2)
US Guided ONSD suggestive of raised ICP	40 (83.33)
GCS with US Guided ONSD suggestive of raised ICP	
≤ 12	36/42 (85.7)

Table-2: US guided ONSD measurements

Age	ONSD mm Mean (±SD)	ONSD mm Mean (±SD)
< 1 yrs n =8	Patients with signs of raised ICP 3 (37.5%)	Patients with no signs of raised ICP 5 (62.5%)
	4.64 (±0.48)	4.32 (±0.71)
1–10 yrs n = 21	Patients with signs of raised ICP 10 (47.6%)	Patients with no signs of raised ICP 11 (52.4%)
	6.44 (±0.65)	5.03 ±0.82)
>10 yrs n = 19	Patients with signs of raised ICP 13 (68.4%)	Patients with no signs of raised ICP 6 (31.5%)
	6.28 (±0.62)	5.46 (±0.91)

Table-3: Sensitivity and specificity of US Guided ONSD measurement based on ROC curves

Characteristics	Sensitivity	Specificity
Age < 1 yrs		
ONSD = 3.96mm	100%	60%
Age 1 - 10yrs		
ONSD = 4.71mm	100%	63.6%
Age > 10 yrs		
ONSD = 5.43mm	100%	66.7%

DISCUSSION

The range of ONSD in normal paediatric population had been described in a number of previous studies. In US, 67 children were recruited and they had used threshold of ultrasonographic ONSD in infants >4 mm and in children >1 year >4.5 mm to be considered as a sign of raised ICP.[14] In UK, 102 normal children, Ultrasonographic ONSD ranged from 2.1 to 4.3 mm with ONSD >4 mm in infants and >4.5 mm in children >1 yr was considered and regarded as abnormal.[18] Another German study including 483 children concludes that Ultrasonographic ONSD >4.5 mm was definitely pathologic and requires further investigation.[17] In 7 African children with no signs of raised ICP, the range of Ultrasonographic ONSD was 2.8 to 4.4 mm with ONSD ≥4.5 mm was considered as a sign of raised ICP.[15] In Irani 78 children, the control group showed the range of 2–4 mm and 2.8–4.35 in <4 years of age and >4 years of age respectively.[20] In Bangladeshi cohort, 136 healthy participants with age ≥4 years and adults had given a range of 4.24–4.83 mm and considered >4.75 mm as abnormal.[16] However, different studies showed the Ultrasonographic ONSD range of 2.9–4.3 mm in 20 German adults,[21] 2.5–4.1 mm in 50 UK adults,[22] and 2.2–4.9 mm in 26 Greek adults.[23] Most of the previous studies in adults showed Ultrasonographic ONSD of greater than 5mm to 5.9 mm as a sign of raised ICP.[12, 23–28] Considering the above mentioned data we considered Ultrasonographic ONSD in infants less than 1 yr. >4 mm, in children 1–10 yrs. >4.5 mm, and in adolescence greater than 1> yrs. >5 mm as a threshold for the identification of raised ICP.

Our study showed the mean age of 7.5 years (±5 years) which was similar to the German cohort.[17]

However, the mean age was lower in African[15] and Irani[20] cohort, and slightly higher in US[14] children. We also report the male preponderance in our study similar to US[14] and Irani[20] children. Our study showed Nontraumatic coma with meningeoencephalitis and stroke being the most common diagnosis which do correlate with the African cohort.[15] However, Irani[20] and US[14] cohort showed the preponderance of head trauma, brain tumor, and Ventriculoperitoneal shunt malfunction.

We report the mean ONSD with signs of raised ICP in infants 4.64 (±0.48), in 1–10 years 6.44 (±0.65), and in adolescent >10 years 6.28 (±0.62) ONSD respectively which is greater than the cut off in infants greater than 4 mm, in children >1 yr. >4.5 mm, and in adults >5 mm as mentioned in previous studies.[12,14-18,23-27] We report the Sensitivity of Ultrasonographic ONSD suggestive of raised ICP 65% which is much lower as compared to the other paediatric cohorts ranging from 83–100%,[14,15] with specificity of 100% greater than African[15] cohort 86% and US[14] cohort 38%. However, when we plotted the ROC curves at various age groups as in figure 3, we found different threshold for the Ultrasonographic ONSD suggestive of raised ICP in different age groups as mentioned in table 3, with sensitivity reaching 100% and specificity declining to 60–66.7%. Also the threshold for children age >1 yrs as shown in table 3, was lower as compared to the African[15] cohort with mean Ultrasonographic ONSD 5.4 mm (range 4.3–6.2 mm) with raised ICP, Irani[20] cohort with mean ONSD, age <4 years and > 4 years, 5.55 mm (±0.68) and 5.68 mm (±0.71), respectively with raised ICP, and in German cohort[17] with mean ONSD of 5.6 mm (±0.9) with raised ICP. Therefore, we recommend the threshold of Ultrasonographic ONSD > 4 mm in infants, >4.71 in children age 1–10 yrs, and > 5.43 mm in adolescent age >10 yrs for the identification of raised ICP.

In almost all patients, we had measured Ultrasonographic ONSD measurement with head end elevated at 30 degrees which is one of the neuroprotective measures in these critically ill neurological patients. Whether, there will be any differences in ONSD measurement with respect to the head end at 0^{o}, 30^{o}, 60^{o} in the same patients at the same point in time, opens another area of research to identify the optimum threshold for raised ICP among children with different age groups.

However, this non-invasive method can safely and rapidly provide information of ICP at bedside and can be frequently repeated. It also allows the observer to quickly assess the ICP variation, which is very important in these clinical scenarios, in the evaluation and follow-up of these patients, where invasive monitoring devices are not available or contraindicated. Thus, Ultrasonographic ONSD measurement in combination with raised ICP clinical signs can be used to identify raised ICP in such scenarios.

Also, invasive monitoring is considered as gold standard and standard reference to compare the other modalities, but differences in the type of invasive ICP monitoring devices, site of insertion (Intraparenchymal, Intraventricular, subdural, epidural), location of tip at different places inside the skull with respect to different site of insertion also makes it difficult to accurately monitor the exact ICP especially in case with the localised disease process.

The reader of this study needs to know that there were several limitations while interpreting this study. In our cohort we used clinical signs of raised ICP as a surrogate marker of raised ICP, as direct invasive monitoring which is considered as gold standard is not frequently performed and recruiting the patients with subject to invasive ICP monitoring was not feasible. Also most of our patients had undergone CT scan brain with few MRI brain within 2 hrs of Ultrasonographic ONSD measurement, but CT scan has been considered as a poor surrogate marker to identify raised ICP.[7,8] Even with normal CT scan brain, the chances of raised ICP ranges from 0–88%.[9] Also in our cohort with radiological imaging, only 29% (14/48) of patients had shown signs of raised ICP, although these number also included 9 MRI brain which has far better sensitivity and specificity for diagnosing raised ICP.

With different operator for Ultrasonographic ONSD measurement, there can be operator bias as ultrasonography is highly operator dependant. Despite of extensive efforts during the training of the operators (Intensive care physicians and fellows) to standardise the image capturing, with optic nerve in the centre of the screen and measurement to be taken 3 mm behind the papilla.

In our cohort, the sample size was small especially in infants. Therefore, larger prospective study would be needed among children with different age groups to establish the accurateness of Ultrasonographic ONSD measurement as an acceptable, non-invasive, safe, and easily repeatable screening and diagnostic tool for the diagnosis of raised ICP.

CONCLUSION

We report the threshold of Ultrasonographic ONSD measurement in infants >4.0 mm, in children 1–10 yrs > 4.71 mm, in adolescent >10 yrs >5.43 mm for identifying the raised ICP with sensitivity and specificity of 100% and 60–66.7% respectively. We also Report 85% of patients with GCS ≤12 showing raised ICP with ultrasonographic ONSD measurement. Ultrasonographic ONSD measurement in combination with GCS can be considered a better screening tool for identification of increased ICP especially in a resource limited developing country.

AUTHORS' CONTRIBUTION

NS: Concept and design, acquisition of data, analysis & & interpretation of data, drafting manuscript. AH: Concept of design, questions related to accuracy or integrity of any part of the work appropriately investigated and resolved, final approval of the version to be published. QA, HJ, BS & RS: Data collection and analysis, interpretation of data.

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